

09/267511

FILE 'REGISTRY' ENTERED AT 10:29:10 ON 24 FEB 2005
L1 63 SEA ABB=ON PLU=ON SALLRSIPA|NAPVSIPQ/SQSP

FILE 'CAPLUS' ENTERED AT 10:29:25 ON 24 FEB 2005
L2 63 SEA ABB=ON PLU=ON L1
L3 24 SEA ABB=ON PLU=ON L2 AND ((FET## OR FOET##) (W) (ALC OR
ALCOHOL) (W) SYNDROM? OR FAS(S) SYNDROM? OR (NEURON? OR NERV###) (5
A) (CELL DEATH OR APOPTOSIS OR APOPTOT?))

L3 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Nov 2004
ACCESSION NUMBER: (2004)1001032 CAPLUS
DOCUMENT NUMBER: 142:17815
TITLE: Neuroprotective effect of activity-dependent
neurotrophic factor against toxicity from familial
amyotrophic lateral sclerosis-linked mutant SOD1 in
vitro and in vivo
AUTHOR(S): Chiba, Tomohiro; Hashimoto, Yuichi; Tajima, Hirohisa;
Yamada, Marina; Kato, Rikiya; Niikura, Takako;
Terashita, Kenzo; Schulman, Howard; Aiso, Sadakazu;
Kita, Yoshiko; Matsuoka, Masaaki; Nishimoto, Ikuro
CORPORATE SOURCE: Department of Pharmacology, KEIO University School of
Medicine, Tokyo, Japan
SOURCE: Journal of Neuroscience Research (2004), 78(4),
542-552
CODEN: JNREDK; ISSN: 0360-4012
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amyotrophic lateral sclerosis (ALS) is the most common fatal motor neuron
disease, affecting mostly middle-aged people. There are no curative
therapies for ALS. Several lines of evidence have supported the notion
that the proapoptotic property of familial ALS (FALS)-linked mutant
Cu/Zn-superoxide dismutase-1 (SOD1) genes may play an important role in
the pathogenesis of some FALS cases. Here we found that
activity-dependent neurotrophic factor (ADNF), a neurotrophic factor
originally identified to have the anti-Alzheimer's disease (AD) activity,
protected against **neuronal cell death** caused
by FALS-linked A4T-, G85R- and G93A-SOD1 in a dose-responsive fashion.
Notably, ADNF-mediated complete suppression of SOD1 mutant-induced
neuronal cell death occurs at concns. as low
as 100 fM. ADNF maintains the neuroprotective activity even at concns. of
more than 1 nM. This is in clear contrast to the previous finding that
ADNF loses its protective activity against neurotoxicity induced by
AD-relevant insults, including some familial AD genes and amyloid β
peptide at concns. of more than 1 nM. Characterization of the
neuroprotective activity of ADNF against cell death caused by SOD1 mutants
revealed that CaMKIV and certain tyrosine kinases are involved in
ADNF-mediated neuroprotection. Moreover, in vivo studies showed that
intracerebroventricularly administered ADNF significantly improved motor
performance of G93A-SOD1 transgenic mice, a widely used model of FALS,
although survival was extended only marginally. Thus, the neuroprotective
activity of ADNF provides a novel insight into the development of curative
drugs for ALS.
IT 177718-96-6, Activity-dependent neurotropic factor peptide-9
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action);

09/267511

PAC (Pharmacological activity); BIOL (Biological study)
(activity-dependent neurotrophic factor neuroprotective effect against
toxicity from familial amyotrophic lateral sclerosis-linked mutant SOD1
in vitro and in vivo)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 07 Jun 2004

ACCESSION NUMBER: 2004:454464 CAPLUS

DOCUMENT NUMBER: 141:64409

TITLE: Protective peptides that are orally active and
mechanistically nonchiral

AUTHOR(S): Brenneman, Douglas E.; Spong, Catherine Y.; Hauser,
Janet M.; Abebe, Daniel; Pinhasov, Albert; Golian,
Tania; Gozes, Illana

CORPORATE SOURCE: Section on Developmental and Molecular Pharmacology,
Laboratory of Developmental Neurobiology, National
Institute of Child Health and Human Development,
National Institutes of Health, Bethesda, MD, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics
(2004), 309(3), 1190-1197
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental
Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous reports identified two peptides that mimic the action of
neuroprotective proteins derived from astrocytes. These peptides,
NAPVSIPQ and SALLRSIPA, prevent **neuronal cell**
death produced by elec. blockade, N-methyl-D-aspartate, and
 β -amyloid peptide (25-35). In the present study, all D-amino acid
peptides of NAPVSIPQ and SALLRSIPA were synthesized and compared resp. to
the corresponding all L-amino acid peptides. In rat cerebral cortical
test cultures cotreated with 1 μ M tetrodotoxin, the D-amino acid
peptides produced similar potency and efficacy for neuroprotection as that
observed for their resp. L-amino acid peptides. Since all these peptides
tested individually exhibited attenuation of efficacy at concns. of > 10
pM, combinations of these peptides were tested for possible synergies.
Equimolar D-NAPVSIPQ and D-SALLRSIPA combination treatment produced potent
neuroprotection (EC₅₀, 0.03 fM) that did not attenuate with increasing
concns. Similarly, the combination of L-NAPVSIPQ and D-SALLRSIPA also had
high potency (EC₅₀, 0.07 fM) without attenuation of efficacy. Combined
administration of peptides was tested in a model of **fetal**
alc. syndrome and in a model of learning impairment:
apolipoprotein E knockout mice. I.p. administration of D-NAPVSIPQ plus
D-SALLRSIPA to pregnant mice (embryonic day 8) attenuated fetal demise
after treatment with an acute high dose of alc. Furthermore, oral
administration of D-NAPVSIPQ plus D-SALLRSIPA significantly increased
fetal survival after maternal alc. treatment. Apolipoprotein E knockout
mice injected with D-NAPVSIPQ plus D-SALLRSIPA showed improved performance
in the Morris water maze. These studies suggest therapeutic potential for
the combined administration of neuroprotective peptides that can act
through a mechanism independent of chiral recognition.

IT 177718-96-6 211439-12-2, NAPVSIPQ 327157-61-9
327157-62-0

Searcher : Shears 571-272-2528

09/267511

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective peptides that are orally active and mechanistically nonchiral)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 07 Jun 2004

ACCESSION NUMBER: 2004:454463 CAPLUS

DOCUMENT NUMBER: 141:201591

TITLE: Ethanol antagonist peptides: Structural specificity without stereospecificity

AUTHOR(S): Wilkemeyer, Michael F.; Chen, Shao-yu; Menkari, Carrie E.; Sulik, Kathleen K.; Charness, Michael E.

CORPORATE SOURCE: Neurology Service, Veterans Affairs Boston Healthcare System, MA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(3), 1183-1189

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Increasing evidence suggests that ethanol damages the developing nervous system partly by disrupting the L1 cell adhesion mol. Ethanol inhibits L1-mediated cell adhesion, and compds. that antagonize this action also prevent ethanol-induced embryotoxicity. Two such compds. are the small peptides NAPVSIPQ (NAP) and SALLRSIPA (SAL). The authors showed previously that NAP and SAL antagonize ethanol inhibition of L1 adhesion at femtomolar to picomolar concns. Here the authors show that, despite this extraordinary potency, both NAP and SAL lack stereospecificity. D-NAP, a peptide composed entirely of D-amino acids, was an effective ethanol antagonist in NIH/3T3 cells transfected with human L1 and in the NG108-15 neural cell line. Interestingly, Ala-substituted derivs. of D-NAP demonstrate the same structure-activity relation as the corresponding derivs. of L-NAP. The Ser-Ile-Pro motif was important for the ethanol antagonist activity of D-NAP, L-NAP, and L-SAL, with Ile being the most critical element in all three. Like L-NAP, D-NAP effectively reduced ethanol-induced growth retardation in mouse whole embryo culture. The potential resistance of D-peptides to proteases makes D-NAP a potentially attractive agent for the prevention of **fetal alc. syndrome**.

IT 177718-96-6 211439-12-2, NAPVSIPQ 327157-61-9
327157-62-0

RL: PAC (Pharmacological activity); BIOL (Biological study)
(ethanol antagonist peptides are structurally specific but not stereospecific)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 08 Oct 2003

ACCESSION NUMBER: 2003:786849 CAPLUS

DOCUMENT NUMBER: 140:37325

TITLE: The role of activity-dependent neuroprotective protein

Searcher : Shears 571-272-2528

09/267511

in a mouse model of **fetal alcohol syndrome**
AUTHOR(S): Poggi, Sarah H.; Goodwin, Katie; Hill, Joanna M.;
Brenneman, Douglas E.; Tendi, Elizabetta; Schinelli,
Sergio; Abebe, Daniel; Spong, Catherine Y.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Georgetown
Univ. Hosp., National Institutes of Health, Bethesda,
DC, USA
SOURCE: American Journal of Obstetrics and Gynecology (2003),
189(3), 790-793
CODEN: AJOGAH; ISSN: 0002-9378
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: **Fetal alc. syndrome (FAS)**
) is the most common nongenetic cause of mental retardation. Peptides
NAPVSIQ (NAP) and SALLRSIPA (SAL), related to activity-dependent
neuroprotective protein (ADNP), prevent alc.-induced damage in a mouse
model of FAS. Our objective was to characterize ADNP in this model to
relate this protein to the mechanisms of damage and peptide
neuroprotection. Study design: Timed, pregnant C57Bl6/J mice were treated
on day 8. Groups were control, alc., peptide pretreatment, or peptide
alone. Embryo and decidua were harvested at 6 and 24 h and 10 days. To
evaluate ADNP expression, real-time polymerase chain reaction was
performed with results presented as the ratio of ADNP-to-glyceraldehyde-3-
phosphate dehydrogenase (GAPDH) concentration. Anal. of variance was
performed

for overall comparisons with $P < 0.05$ considered significant. Results: At
6 h, there was no difference in ADNP between alc.-exposed embryos compared
with control embryos. At 24 h, there was an increase in ADNP in
alc.-exposed embryos compared with controls ($P < 0.001$); these findings
persisted at 10 days ($P < 0.001$). In the decidua at 6 h, there was no
difference between alc. and control. At 24 h, there was greater ADNP in
alc.-exposed decidua compared with controls ($P < 0.001$), which did not
persist at 10 days ($P = 0.97$). Peptide pretreatment did not prevent the
alc.-induced increase in ADNP in embryo or decidua. Conclusion: Alc.
increased embryonic and decidual ADNP expression at 24 h and it persisted
in the embryo for 10 days. Because ADNP is a known neuroprotectant, these
findings suggest that it may be released as a protective mechanism in FAS.
Changes in the embryo were persistent suggesting that the embryo is more
vulnerable to alc.-induced damage than the mother.

IT 177718-96-6 211439-12-2, NAPVSIQ
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(activity-dependent neuroprotective protein role in mouse model of
fetal alc. syndrome)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 03 Oct 2003

ACCESSION NUMBER: 2003:775826 CAPLUS

DOCUMENT NUMBER: 140:36048

TITLE: From vasoactive intestinal peptide (VIP) through
activity-dependent neuroprotective protein (ADNP) to
NAP. A view of neuroprotection and cell division

Searcher : Shears 571-272-2528

09/267511

AUTHOR(S): Gozes, Illana; Divinsky, Inna; Pilzer, Inbar; Fridkin, Mati; Brenneman, Douglas E.; Spier, Avron D.
CORPORATE SOURCE: Department of Clinical Biochemistry, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel
SOURCE: Journal of Molecular Neuroscience (2003), 20(3), 315-322
CODEN: JMNEES; ISSN: 0895-8696
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Accelerated neuronal death brings about cognitive as well as motor and other dysfunctions. A major neuropeptide, vasoactive intestinal peptide (VIP), has been shown to be neuroprotective. However, VIP-based drug design is hampered by the instability of the peptide and its limited bioavailability. Two independent approaches were thus taken to exploit VIP as a lead drug candidate: (1) potent neuroprotective lipophilic analogs of VIP were synthesized, e.g. [stearyl-norleucine-17] VIP (SNV); and (2) potent neuroprotective peptide derivs. were identified that mimic the activity of VIP-responsive neuroprotective glial proteins. VIP provides neuronal defense by inducing the synthesis and secretion of neuroprotective proteins from astrocytes; activity-dependent neuroprotective protein (ADNP) was discovered as such glial cell mediator of VIP- and SNV-induced neuroprotection. In subsequent studies, an eight-amino-acid peptide, NAP, was identified as the smallest active element of ADNP exhibiting potent neuroprotective activities. This paper summarizes the biol. effects of SNV and NAP and further reports advances in NAP studies toward clin. development. An original finding described here shows that NAP, while protecting neurons, demonstrated no apparent effect on cell division in a multiplicity of cell lines, strengthening the notion that NAP is a specific neuroprotective drug candidate.

IT 211439-12-2

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VIP, activity-dependent neuroprotective protein ADNP and NAP in relation to neuroprotection and cell division)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 04 Sep 2003

ACCESSION NUMBER: 2003:688962 CAPLUS

DOCUMENT NUMBER: 139:208245

TITLE: Mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of neuronal cell death

INVENTOR(S): Gozes, Illana; Brenneman, Douglas E.; Bassan, Merav; Zamostiano, Rachel

PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development Ltd., Israel; The United States of America, Department of Health and Human Services
SOURCE: U.S., 105 pp., Cont.-in-part of Appl. No. PCT/US98/02485.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

Searcher : Shears 571-272-2528

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6613740	B1	20030902	US 1998-187330	19981106
WO 9835042	A2	19980813	WO 1998-US2485	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2349159	AA	20000518	CA 1999-2349159	19991104
WO 2000027875	A2	20000518	WO 1999-US26213	19991104
WO 2000027875	A3	20000727		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1124960	A2	20010822	EP 1999-971817	19991104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 776833	B2	20040923	AU 2000-14698	19991104
US 2004053313	A1	20040318	US 2003-623272	20030717
PRIORITY APPLN. INFO.:				
			US 1997-37404P	P 19970207
			WO 1998-US2485	A2 19980206
			US 1998-187330	A 19981106
			WO 1999-US26213	W 19991104

OTHER SOURCE(S): MARPAT 139:208245

AB The present invention relates generally to Activity Dependent Neurotrophic Factor III (ADNF III), also known as Activity Dependent Neuroprotective Protein (ADNP). More particularly, the present invention relates to nucleic acid sequences encoding ADNF III polypeptides; ADNF III polypeptides encoded by such nucleic acid sequences; antibodies to ADNF III polypeptides; and methods of using such ADNF III polypeptides for the treatment of neurol. deficiencies and for the prevention of cell death associated with (1) gp120, the envelope protein from HIV; (2) N-methyl-D-aspartic acid (excito-toxicity); (3) tetrodotoxin (blockage of elec. activity); and (4) β -amyloid peptide, a substance related to neuronal degeneration in Alzheimer's disease. The mouse and human ADNF III cDNAs were cloned and sequenced. An ADNF III-derived octapeptide, NAPVSIPQ, mimicked the activity of the total protein in a neurodegeneration model system (ApoE-deficient homozygous mice) and a rat model of cholinergic deficiency. Claimed sequences are inadequately identified in the document.

IT 590465-44-4D, N- and C-terminal extension derivs.
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence, activity-dependent neurotrophic factor III; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT 590465-45-5 590465-46-6 590465-47-7
590465-48-8 590465-49-9

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT 177159-38-5 177718-96-6 211439-10-0
211439-12-2 270084-37-2 270084-38-3
292039-06-6 292039-07-7 292039-08-8
590516-42-0 590516-43-1 590516-45-3

RL: PRP (Properties)
(unclaimed protein sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 21 Jul 2003

ACCESSION NUMBER: 2003:555487 CAPLUS

DOCUMENT NUMBER: 139:209175

TITLE: Differential effects of ethanol antagonism and neuroprotection in peptide fragment NAPVSIPQ prevention of ethanol-induced developmental toxicity
AUTHOR(S): Wilkemeyer, Michael F.; Chen, Shao-yu; Menkari, Carrie E.; Brenneman, Douglas E.; Sulik, Kathleen K.; Charness, Michael E.

CORPORATE SOURCE: Veterans Affairs Boston Healthcare System, Neurology Service, West Roxbury, MA, 02132, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(14), 8543-8548
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB NAPVSIPQ (NAP), an active fragment of the glial-derived activity-dependent neuroprotective protein, is protective at femtomolar concns. against a wide array of neural insults and prevents ethanol-induced fetal wastage and growth retardation in mice. NAP also antagonizes ethanol inhibition of L1-mediated cell adhesion (ethanol antagonism). We performed an Ala scanning substitution of NAP to determine the role of ethanol antagonism and neuroprotection in NAP prevention of ethanol embryotoxicity. The Ser-Ile-Pro region of NAP was crucial for both ethanol antagonism and protection of cortical neurons from tetrodotoxin toxicity (neuroprotection). Ala replacement of either Ser-5 or Pro-7 (P7A-NAP) abolished NAP neuroprotection but minimally changed the efficacy of NAP ethanol antagonism. In contrast, Ala replacement of Ile-6 (I6A-NAP) caused a decrease in potency (>2 logarithmic orders) with only a small reduction (<10%) in the efficacy of NAP neuroprotection but markedly reduced the efficacy (50%) and the potency (5 logarithmic orders) of NAP ethanol antagonism. Ethanol significantly reduced the number of paired somites in

mouse whole-embryo culture; this effect was prevented significantly by 100 pM NAP or by 100 pM P7A-NAP, but not by 100 pM I6A-NAP. The structure-activity relation for NAP prevention of ethanol embryotoxicity was similar to that for NAP ethanol antagonism and different from that for NAP neuroprotection. These findings support the hypothesis that NAP antagonism of ethanol inhibition of L1 adhesion plays a central role in NAP prevention of ethanol embryotoxicity and highlight the potential importance of ethanol effects on L1 in the pathophysiol. of **fetal alc. syndrome**.

IT 211439-12-2, NAPVSIPQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(differential effects of ethanol antagonism and neuroprotection in peptide fragment NAPVSIPQ prevention of ethanol-induced developmental toxicity in human L1-transfected NIH/3T3 cells)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 03 Oct 2002

ACCESSION NUMBER: 2002:749911 CAPLUS

DOCUMENT NUMBER: 138:282681

TITLE: Peptide antagonists of ethanol inhibition of L1-mediated cell-cell adhesion

AUTHOR(S): Wilkemeyer, Michael F.; Menkari, Carrie E.; Spong, Catherine Y.; Charness, Michael E.

CORPORATE SOURCE: Department of Neurology, Brigham and Women's Hospital, Boston, MA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 303(1), 110-116
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ethanol inhibits cell-cell adhesion mediated by the L1 cell adhesion mol. 1-Octanol potentially antagonizes this cellular action of ethanol and also prevents ethanol-induced dysmorphol. and cell death in mouse whole embryo culture. NAPVSIPQ (NAP) and SALLRSIPA (SAL) are active peptide fragments of two neuroprotective proteins: activity-dependent neuroprotective protein and activity-dependent neurotrophic factor. NAP and SAL are neuroprotective at femtomolar concns. against a variety of neurotoxins and also prevent ethanol teratogenesis in mice. To explore the cellular basis for this action, we asked whether NAP and SAL antagonize ethanol inhibition of L1 adhesion. Aggregation assays were carried out in ethanol-sensitive, human L1-transfected NIH/3T3 cells in the absence and presence of NAP and SAL. Neither NAP nor SAL altered L1 adhesion or L1 expression; however, both peptides potentially and completely antagonized the inhibition of L1 adhesion by 100 mM ethanol (EC50: NAP, 6+10-14 M; SAL, 4+10-11 M). NAP also antagonized ethanol inhibition of cell-cell adhesion in bone morphogenetic protein-7-treated NG108-15 cells. In L1-expressing NIH/3T3 cells, SAL antagonism was reversible and could be overcome by increasing concns. of ethanol. In contrast, NAP antagonism was irreversible and could not be overcome by increasing agonist concentration

Two scrambled NAP peptides (ASPNQPIV and PNIQVASP) were not antagonists at

concns. as high as 10^{-7} M. Thus, two structurally unrelated classes of compds., alcs. and small polypeptides, share two common actions: antagonism of ethanol inhibition of L1-mediated cell adhesion and prevention of ethanol teratogenesis. These findings support the hypothesis that ethanol inhibition of L1 adhesion contributes to ethanol teratogenesis.

IT **211439-12-2**, NAPVSIPQ

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NAP peptide; peptide antagonists of ethanol inhibition of L1-mediated cell-cell adhesion)

IT **177718-96-6**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SAL peptide; peptide antagonists of ethanol inhibition of L1-mediated cell-cell adhesion)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 28 Aug 2001

ACCESSION NUMBER: 2001:623335 CAPLUS

DOCUMENT NUMBER: 135:299083

TITLE: Neurotrophins prevent HIV Tat-induced **neuronal apoptosis** via a nuclear factor- κ B (NF- κ B)-dependent mechanism

AUTHOR(S): Ramirez, Servio H.; Sanchez, Joseph F.; Dimitri, Christopher A.; Gelbard, Harris A.; Dewhurst, Stephen; Maggirwar, Sanjay B.

CORPORATE SOURCE: Departments of Microbiology and Immunology, University of Rochester Medical Center, Rochester, NY, 14642, USA

SOURCE: Journal of Neurochemistry (2001), 78(4), 874-889
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB HIV-1 associated dementia is thought to be caused by neuronal damage and death in response to the production of soluble neurotoxic factors by virally infected mononuclear phagocytes. These neurotoxins include HIV-1 Tat. The ability of neurotrophins to promote cell survival prompted the authors to examine whether neurotrophins might also be capable of opposing the pro-apoptotic effects of Tat. Here, the authors show that Tat-induced **neuronal apoptosis** in primary cultures of rat cerebellar granule cells and in neuronally differentiated human SK-N-MC cells is profoundly inhibited by brain-derived neurotrophic factor, nerve growth factor and activity-dependent neurotrophic factor nonamer peptide. These neurotrophins activated the transcription factor NF- κ B, and inhibition of NF- κ B activation using a super-repressor I κ B- α mutant was found to block the survival-promoting activity of the neurotrophins. Reporter gene assays and immunoblot expts. revealed that the neurotrophins also up-regulated the expression of Bcl-2, at both the transcriptional and protein levels. Overexpression of the super-repressor I κ B- α mutant prevented this induction of Bcl-2 expression. Moreover, overexpression of either Bcl-2, alone, or the RelA subunit of NF- κ B, alone, protected **neurons** from Tat-induced **apoptosis**. These findings suggest that the

activation of NF- κ B by neurotrophic factors may promote survival of neurons exposed to Tat, via regulation of anti-apoptotic genes including Bcl-2.

IT 177718-96-6, Activity-dependent neurotrophic factor peptide 9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (neurotrophins prevent HIV Tat-induced **neuronal apoptosis** via a nuclear factor- κ B-dependent mechanism)
 REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 07 May 2001

ACCESSION NUMBER: 2001:321648 CAPLUS

DOCUMENT NUMBER: 134:362624

TITLE: Prevention of fetal demise and growth restriction in a mouse model of **fetal alcohol syndrome**

AUTHOR(S): Spong, Catherine Y.; Abebe, Daniel T.; Gozes, Illana; Brenneman, Douglas E.; Hill, Joanna M.

CORPORATE SOURCE: Section on Developmental and Molecular Pharmacology, Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 297(2), 774-779

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two peptides [NAPVSIPQ (NAP) and SALLRSIPA (ADNF-9)], that are associated with novel glial proteins regulated by vasoactive intestinal peptide, are shown now to provide protective intervention in a model of **fetal alc. syndrome**. Fetal demise and growth restrictions were produced after the i.p. injection of ethanol to pregnant mice during mid-gestation (E8). Death and growth abnormalities elicited by alc. treatment during development are believed to be associated, in part, with severe oxidative damage. NAP and ADNF-9 have been shown to exhibit antioxidative and antiapoptotic actions in vitro. Pretreatment with an equimolar combination of the peptides prevented the alc.-induced fetal death and growth abnormalities. Pretreatment with NAP alone resulted in a significant decrease in alc.-associated fetal death; whereas ADNF-9 alone

had

no detectable effect on fetal survival after alc. exposure, indicating a pharmacol. distinction between the peptides. Biochem. assessment of the fetuses indicated that the combination peptide treatment prevented the alc.-induced decreases in reduced glutathione. Peptide efficacy was evident with either 30-min pretreatment or with 1-h post-alc. administration. Bioavailability studies with [3H]NAPVSIPQ indicated that 39% of the total radioactivity comigrated with intact peptide in the fetus 60 min after administration. These studies demonstrate that fetal death and growth restriction associated with prenatal alc. exposure were prevented by combinatorial peptide treatment and suggest that this therapeutic strategy be explored in other models/diseases associated with oxidative stress.

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IT 211439-12-2, NAPVSIPO

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(prevention of fetal demise and growth restriction in mouse model of fetal alc. syndrome)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 25 Feb 2001

ACCESSION NUMBER: 2001:137237 CAPLUS

DOCUMENT NUMBER: 134:198025

TITLE: Orally active peptides that prevent cell damage and death

INVENTOR(S): Brenneman, Douglas E.; Gozes, Illana; Spong, Catherine Y.; Pinhasov, Albert; Giladi, Eliezer

PATENT ASSIGNEE(S): Ramot University Authority for Applied Research & Industrial Development, Israel; United States Dept. of Health and Human Services

SOURCE: PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012654	A2	20010222	WO 2000-US22861	20000817
WO 2001012654	A3	20020124		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2381981	AA	20010222	CA 2000-2381981	20000817
AU 2000069201	A5	20010313	AU 2000-69201	20000817
AU 761597	B2	20030605		
EP 1206489	A2	20020522	EP 2000-957607	20000817
EP 1206489	B1	20040506		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
AT 266044	E	20040515	AT 2000-957607	20000817
ES 2220522	T3	20041216	ES 2000-957607	20000817
PRIORITY APPLN. INFO.:			US 1999-149956P	P 19990818
			WO 2000-US22861	W 20000817

AB This invention provides an ADNF (activity-dependent neurotrophic factor) polypeptide comprising an active core site, the active core site comprising at least one D-amino acid. The invention also provides a pharmaceutical composition comprising an ADNF polypeptide comprising an active core site, the active core site comprising at least one D-amino acid. In

Searcher : Shears 571-272-2528

09/267511

particular, the pharmaceutical composition of the invention is orally active.

The invention further provides methods for reducing **neuronal cell death**, methods for reducing oxidative stress, and methods for reducing a condition associated with **fetal alc . syndrome** using the ADNF polypeptides and the pharmaceutical compns. of the invention.

IT 177159-38-5 177718-96-6 209051-20-7
209051-27-4 211439-10-0 211439-12-2
292039-03-3 292039-04-4 292039-05-5
292039-06-6 292039-07-7 292039-08-8
327157-61-9 327157-62-0 327157-63-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(orally active peptides that prevent cell damage and death)

L3 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 19 Jan 2001

ACCESSION NUMBER: 2001:45165 CAPLUS

DOCUMENT NUMBER: 134:120910

TITLE: Neurotrophic peptides of activity-dependent neurotrophic factor

INVENTOR(S): Brenneman, Douglas E.

PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development, Israel; The United States of America as Represented by the Department of Health and Human Services

SOURCE: U.S., 32 pp., Cont.-in-part of U.S. 5,767,240.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6174862	B1	20010116	US 1994-324297	19941017
US 688087	A0	19920101	US 1991-688087	19910422
US 5767240	A	19980616	US 1992-871973	19920422
CA 2202496	AA	19960425	CA 1995-2202496	19951016
WO 9611948	A1	19960425	WO 1995-US12929	19951016
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9537641	A1	19960506	AU 1995-37641	19951016
AU 707838	B2	19990722		
EP 797590	A1	19971001	EP 1995-935735	19951016
EP 797590	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10509428	T2	19980914	JP 1995-513344	19951016
AT 212359	E	20020215	AT 1995-935735	19951016

Searcher : Shears 571-272-2528

09/267511

PRIORITY APPLN. INFO.:

US 1991-688087 B2 19910422
US 1992-871973 A2 19920422
US 1994-324297 A 19941017
WO 1995-US12929 W 19951016

OTHER SOURCE(S): MARPAT 134:120910

AB The present invention relates generally to Activity-Dependent Neurotrophic Factor (ADNF). More particularly, the present invention relates to a family of polypeptides derived from ADNF that exhibit neuroprotective/neurotrophic action on neurons originating in the central nervous system and to uses thereof for the treatment of neurol. deficiencies and for the prevention of cell death. The present invention also relates to pharmaceutical compns. designed to prevent neuronal cell death.

IT 177159-38-5 177718-96-6 209051-20-7
209051-27-4 320609-76-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(neurotrophic peptides of activity-dependent neurotrophic factor)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 15 Sep 2000

ACCESSION NUMBER: 2000:645879 CAPLUS

DOCUMENT NUMBER: 133:233267

TITLE: Prevention of fetal alcohol syndrome and neuronal cell death with ADNF polypeptides

INVENTOR(S): Brenneman, Douglas E.; Spong, Catherine Y.; Gozes, Illana; Bassan, Merav; Zamostiano, Rachel

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Ramot of Tel Aviv University

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053217	A2	20000914	WO 2000-US6364	20000310
WO 2000053217	A3	20010111		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002111301	A1	20020815	US 1999-267511	19990312
PRIORITY APPLN. INFO.:			US 1999-267511	A 19990312

Searcher : Shears 571-272-2528

AB The invention relates to methods for reducing a condition associated with **fetal alc. syndrome** in a subject who is exposed to alc. in utero with an ADNF (activity dependent neurotrophic factors) polypeptide (e.g, ADNF I polypeptides, ADNF III polypeptides, or mixts. of ADNF I and ADNF III polypeptides). The ADNF polypeptide of the invention is selected from the group consisting of: (a) an ADNF I polypeptide comprising an active core site having the following amino acid sequence: Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala (SEQ ID NO: 1); (b) an ADNF III polypeptide comprising an active core site having the following amino acid sequence: Asn-Ala-Pro-Val-Ser-Ile-Pro-Gln (SEQ ID NO:2); and (c) a mixture of the ADNF I polypeptide of part (a) and the ADNF III polypeptide of part (b). The **fetal alc. syndrome** condition that is treated is decreased body weight, decreased brain weight, decreased level of VIP mRNA or protein, decreased viability, or decreased learning. The present invention further relates to methods for reducing **neuronal cell death** by contacting **neuronal** cells with a mixture of ADNF I and ADNF III polypeptides. At least one of the ADNF polypeptides can be encoded by a nucleic acid which is administered to the subject. Still further, the present invention relates to a pharmaceutical composition comprising a mixture of

ADNF I
and ADNF III polypeptides.

IT 177159-38-5P 177718-96-6P 209051-20-7P
209051-27-4P 211439-10-0P 211439-12-2P
292039-03-3P 292039-04-4P 292039-05-5P
292039-06-6P 292039-07-7P 292039-08-8P
RL: BAC (Biological activity or effector, except adverse); BPN
(Biosynthetic preparation); BSU (Biological study, unclassified); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(prevention of conditions associated with **fetal alc.
syndrome** and **neuronal cell death**
with ADNF polypeptides)

L3 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 28 Jun 2000

ACCESSION NUMBER: 2000:429944 CAPLUS

DOCUMENT NUMBER: 133:130186

TITLE: Nuclear factor- κ B mediates the cell
survival-promoting action of activity-dependent
neurotrophic factor peptide-9

AUTHOR(S): Glazner, Gordon W.; Camandola, Simonetta; Mattson,
Mark P.

CORPORATE SOURCE: Sanders-Brown Research Center on Aging and Department
of Anatomy and Neurobiology, University of Kentucky,
Lexington, KY, USA

SOURCE: Journal of Neurochemistry (2000), 75(1), 101-108
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) is produced by astrocytes in response to neuronal depolarization and, in turn, promotes neuronal survival. A nine-amino acid ADNF peptide (ADNF9) exhibits full neurotrophic activity and potentially protects cultured embryonic rat hippocampal **neurons** from oxidative injury and **apoptosis**

. Picomolar concns. of ADNF9 induced an increase in nuclear factor- κ B (NF- κ B) DNA-binding activity within 1 h of exposure, with a maximum increase of .apprx.10-fold by 6 h. Activation of NF- κ B was correlated with increased resistance of **neurons** to **apoptosis** induced by exposure to Fe²⁺. The antiapoptotic action of ADNF9 was abolished when NF- κ B activation was specifically blocked with κ B decoy DNA. Oxidative stress was attenuated in neurons pretreated with ADNF9, and this effect of ADNF9 was blocked by κ B decoy DNA, suggesting that ADNF9 suppresses apoptosis by reducing oxidative stress. ADNF9 also prevented **neuronal apoptosis** following trophic factor withdrawal via an NF- κ B-mediated mechanism. Thus, NF- κ B mediates the neuron survival-promoting effects of ADNF9 in exptl. models relevant to developmental neuronal death and neurodegenerative disorders.

IT 177718-96-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(nuclear factor- κ B mediates cell survival-promoting action of activity-dependent neurotrophic factor peptide-9 in rat hippocampal neurons)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 06 Jun 2000

ACCESSION NUMBER: 2000:373753 CAPLUS

DOCUMENT NUMBER: 133:84725

TITLE: Activity-dependent neurotrophic factor: intranasal administration of femtomolar-acting peptides improve performance in a water maze

AUTHOR(S): Gozes, Illana; Giladi, Eliezer; Pinhasov, Albert; Bardea, Amos; Brenneman, Douglas E.

CORPORATE SOURCE: Department of Clinical Biochemistry, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 1091-1098

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) is a glia-derived protein that is neuroprotective at femtomolar concns. A nine-amino acid peptide derived from ADNF (Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala; ADNF-9) captured the activity of the parent protein and has been reported to protect cultured neurons from multiple neurotoxins. Antibodies recognizing ADNF-9 produced **neuronal apoptosis**, and identified an addnl., structurally related, glia-derived peptide, Asn-Ala-Pro-Val-Ser-Ile-Pro-Gln (NAP). Previous comparative studies have characterized s.c.-injected NAP as most efficacious in protecting against developmental retardation and learning impairments in apolipoprotein E-deficient mice. This study was designed to assess (1) neuroprotection after intranasal administration of ADNF-9 and NAP to rats treated with the cholinotoxin ethylcholine aziridium; and (2) bioavailability and pharmacokinetics after intranasal administration. Results showed significant improvements in short-term spatial memory, as assessed in a water maze, after daily intranasal

administration of 1 µg of peptide (ADNF-9 or NAP) per animal. However, a 5-day pretreatment with ADNF-9 did not improve performance measured after cessation of treatment. Compared with rats treated with ADNF-9, NAP-pre-treated animals exhibited a significantly better performance. Furthermore, NAP (and not ADNF-9) protected against loss of choline acetyltransferase activity. Significant amts. of 3H-labeled NAP reached the brain, remained intact 30 min after administration, and dissipated 60 min after administration. This study revealed efficacy for ADNF-related peptides in rodent models for neurodegeneration. The small size of the mols., the low dosage required, the noninvasive administration route, and the demonstrated activity in a relevant paradigm suggest NAP as a lead compound for future drug design.

IT 177718-96-6 211439-12-2

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(activity-dependent neurotrophic factor derivative intranasal administration pharmacokinetics, metabolism and neuroprotection and effect on memory and learning)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 19 May 2000

ACCESSION NUMBER: 2000:335438 CAPLUS

DOCUMENT NUMBER: 133:1200

TITLE: Mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of neuronal cell death

INVENTOR(S): Gozes, Illana; Brenneman, Douglas E.; Bassan, Merav; Zamostiano, Rachel

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Ramot University Authority for Applied Research and Industrial Development

SOURCE: PCT Int. Appl., 136 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027875	A2	20000518	WO 1999-US26213	19991104
WO 2000027875	A3	20000727		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6613740	B1	20030902	US 1998-187330	19981106

09/267511

CA 2349159	AA	20000518	CA 1999-2349159	19991104
EP 1124960	A2	20010822	EP 1999-971817	19991104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 776833	B2	20040923	AU 2000-14698	19991104
PRIORITY APPLN. INFO.:			US 1998-187330	A 19981106
			US 1997-37404P	P 19970207
			WO 1998-US2485	A2 19980206
			WO 1999-US26213	W 19991104

OTHER SOURCE(S): MARPAT 133:1200

AB The present invention relates generally to Activity Dependent Neurotrophic Factor III (ADNF III), also known as Activity Dependent Neuroprotective Protein (ADNP). More particularly, the present invention relates to nucleic acid sequences encoding ADNF III polypeptides; ADNF III polypeptides encoded by such nucleic acid sequences; antibodies to ADNF III polypeptides; and methods of using such ADNF III polypeptides for the treatment of neurol. deficiencies and for the prevention of cell death associated with (1) gp120, the envelope protein from HIV; (2) N-methyl-D-aspartic acid (excito-toxicity); (3) tetrodotoxin (blockage of elec. activity); and (4) β -amyloid peptide, a substance related to neuronal degeneration in Alzheimer's disease. The rat and human ADNF III cDNAs were cloned and sequenced. An ADNF III-derived octapeptide, NAPVSIPQ, mimicked the activity of the total protein in a neurodegeneration model system (ApoE-deficient homozygous mice) and a rat model of cholinergic deficiency. Claimed sequences are inadequately identified in the document.

IT **211439-12-2D**, conjugates

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ADNF III peptide; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **211681-43-5 211681-48-0**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **177159-38-5 177718-96-6 211439-12-2**

223533-74-2 270084-37-2 270084-38-3

270898-03-8 270898-05-0

RL: PRP (Properties)

(unclaimed sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

L3 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 01 Mar 2000

ACCESSION NUMBER: 2000:138163 CAPLUS

DOCUMENT NUMBER: 132:217349

TITLE: Vasoactive intestinal peptide (VIP) prevents
neurotoxicity in neuronal cultures: relevance to
neuroprotection in Parkinson's disease

AUTHOR(S): Offen, Daniel; Sherki, Yossi; Melamed, Eldad; Fridkin,

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Mati; Brenneman, Douglas E.; Gozes, Illana
 Department of Clinical Biochemistry and Felsentein
 Medical Research Center, Rabin Medical Center, The
 Sackler Faculty of Medicine, Department of Neurology
 and Felsentein Medical Research Center, Tel Aviv
 University, Tel Aviv-Jaffa, 69978, Israel

SOURCE: Brain Research (2000), 854(1,2), 257-262
 CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vasoactive intestinal peptide (VIP) provides neuroprotection against β -amyloid toxicity in models of Alzheimer's disease. A superactive analog, stearylNle 17-VIP (SNV) is a 100-fold more potent than VIP. In primary neuronal cultures, VIP protective activity may be mediated by femtomolar-acting glial proteins such as activity-dependent neurotrophic factor (ADNF), activity-dependent neuroprotective protein (ADNP), peptide derivs. ADNF-9 (9aa) and NAP (8aa), resp. It has been hypothesized that β -amyloid induces oxidative stress leading to **neuronal cell death**. Similarly, dopamine and its oxidation products were suggested to trigger dopaminergic nigral cell death in Parkinson's disease. The authors now examined the possible protective effects of VIP against toxicity of dopamine, 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenylpyridinium ion (MPP+) in neuronal cultures [rat pheochromocytoma (PC12), human neuroblastoma (SH-SY5Y) and rat cerebellar granular cells]. Remarkably low concns. of VIP (10⁻¹⁶-10⁻⁸ M), ADNF-9 and NAP (10⁻¹⁸-10⁻¹⁰ M) protected against dopamine and 6-OHDA toxicity in PC12 and neuroblastoma cells. VIP (10⁻¹¹-10⁻⁹ M) and SNV (10⁻¹³-10⁻¹¹ M), protected cerebellar granule neurons against 6-OHDA. In contrast, VIP did not rescue neurons from death associated with MPP+. Since dopamine toxicity is linked to the red/ox state of the cellular glutathione, the authors investigated neuroprotection in cells depleted of reduced glutathione (GSH). Buthionine sulfoximine (BSO), a selective inhibitor of glutathione synthesis, caused a marked reduction in GSH in neuroblastoma cells and their viability decreased by 70-90%. VIP, SNV or NAP (over a wide concentration range)

provided significant neuroprotection against BSO toxicity. These results show that the mechanism of neuroprotection by VIP/SNV/NAP may be mediated through raising cellular resistance against oxidative stress. The authors' data suggest these compds. as potential lead compds. for protective therapies against Parkinson's disease.

IT 177718-96-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (VIP prevention of neurotoxicity in neuronal cultures and involved mechanisms in relation to neuroprotection in Parkinson's disease)

IT 211439-12-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(VIP prevention of neurotoxicity in neuronal cultures and involved mechanisms in relation to neuroprotection in Parkinson's disease)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

09/267511

ED Entered STN: 24 Feb 2000
ACCESSION NUMBER: 2000:127460 CAPLUS
DOCUMENT NUMBER: 132:330286
TITLE: Differential Effects of BDNF, ADNF9, and TNF α on Levels of NMDA Receptor Subunits, Calcium Homeostasis, and Neuronal Vulnerability to Excitotoxicity
AUTHOR(S): Glazner, Gordon W.; Mattson, Mark P.
CORPORATE SOURCE: Sanders-Brown Research Center on Aging and Department of Anatomy and Neurobiology, University of Kentucky, Lexington, KY, 40536, USA
SOURCE: Experimental Neurology (2000), 161(2), 442-452
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Calcium influx through N-methyl-D-aspartate (NMDA) receptors can result in **neuronal apoptosis** or necrosis and may play a pivotal role in neuronal death in many different neurodegenerative diseases. In the present study the authors employed primary neuronal cultures and three different excitoprotective factors, brain-derived neurotrophic factor (BDNF), activity-dependent neurotrophic factor (ADNF9), and tumor necrosis factor α (TNF α), to elucidate the mechanisms whereby trophic factors modify the excitotoxic process. Neurons pretreated with BDNF exhibited increased levels of the NMDA receptor subunits NR1 and NR2A, which was associated with increased calcium responses to NMDA and vulnerability to excitotoxic necrosis and reduced vulnerability to apoptosis. ADNF9 and TNF α suppressed calcium responses to glutamate and protected **neurons** against both excitotoxic necrosis and **apoptosis**, but had no effect on levels of NMDA receptor subunits. Inhibition of phosphorylation and DNA binding of NF- κ B, by H7 and κ B decoy DNA, resp., suggest that the excitotoxic-modulating actions of BDNF are mediated by kinases, while those of ADNF9 and TNF α are mediated by both kinases and the transcription factor NF- κ B. The authors' data show that, whereas BDNF increases neuronal responses to glutamate while ADNF9 and TNF α decrease the same, all three protect against excitotoxic apoptosis. (c) 2000 Academic Press.

IT 177718-96-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(BDNF and ADNF9 and TNF α differential effects on levels of NMDA receptor subunits and calcium homeostasis and neuronal vulnerability to excitotoxicity)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 03 Dec 1999
ACCESSION NUMBER: 1999:763280 CAPLUS
DOCUMENT NUMBER: 132:59555
TITLE: Activity-dependent neurotrophic factor peptide (ADNF9) protects neurons against oxidative stress-induced death
AUTHOR(S): Glazner, Gordon W.; Boland, Andre; Dresse, Albert E.; Brenneman, Douglas E.; Gozes, Illana; Mattson, Mark P.
CORPORATE SOURCE: Sanders-Brown Research Center on Aging and Department of Anatomy and Neurobiology, University of Kentucky,

09/267511

SOURCE: Lexington, KY, 40536-0230, USA
Journal of Neurochemistry (1999), 73(6), 2341-2347
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) and a 14-amino acid fragment of this peptide (sequence VLGGGSALLRSIPA) protect neurons from death associated with an array of toxic conditions, including amyloid β -peptide, N-methyl-D-aspartate, tetrodotoxin, and the neurotoxic HIV envelope coat protein gp 120. The authors report that an even smaller, nine-amino acid fragment (ADNF9) with the sequence SALLRSIPA potentially protects cultured embryonic day 18 rat hippocampal **neurons** from oxidative injury and **neuronal apoptosis** induced by FeSO₄ and trophic factor withdrawal. Among the characteristics of this protection are maintenance of mitochondrial function and a reduction in accumulation of intracellular reactive oxygen species.

IT 177718-96-6, Activity-dependent neurotrophic factor peptide-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activity-dependent neurotrophic factor peptide ADNF9 protects neurons against oxidative stress-induced death).

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 26 Apr 1999

ACCESSION NUMBER: 1999:254850 CAPLUS

DOCUMENT NUMBER: 131:54308

TITLE: A femtomolar-acting neuroprotective peptide induces increased levels of heat shock protein 60 in rat cortical neurons: a potential neuroprotective mechanism

AUTHOR(S): Zamostiano, Rachel; Pinhasov, Albert; Bassan, Merav; Perl, Orly; Steingart, Ruth A.; Atlas, Roy; Brenneman, Douglas E.; Gozes, Illana

CORPORATE SOURCE: Sackler School of Medicine, Department of Clinical Biochemistry, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel

SOURCE: Neuroscience Letters (1999), 264(1,2,3), 9-12

CODEN: NELED5; ISSN: 0304-3940

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) was recently isolated from conditioned media of astrocytes stimulated with VIP. ADNF provided neuroprotection at femtomolar concentration against a wide variety of toxic insults. A nine amino acid peptide (ADNF-9) captured with even greater potency the neuroprotective activity exhibited by the parent protein. Utilizing Northern and Western blot analyses, it was now shown that ADNF-9 increased the expression of heat shock protein 60 (hsp60) in rat cerebral cortical cultures. In contrast, treatment with the Alzheimer's toxin, the β -amyloid peptide, reduced the amount of intracellular hsp60. Treatment with ADNF-9 prevented the reduction in hsp60 produced by the β -amyloid peptide. The protection against the β -amyloid peptide-associated cell death provided by ADNF-9 may be mediated in part by

09/267511

intracellular increases in hsp60.

IT 177718-96-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(activity-dependent neurotrophic factor nanopeptide neuroprotection mediation by increases in HSP60)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 31 Aug 1998

ACCESSION NUMBER: 1998:550513 CAPLUS

DOCUMENT NUMBER: 129:185098

TITLE: Mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of neuronal cell death

INVENTOR(S): Gozes, Illana; Brenneman, Douglas E.; Bassan, Merav

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9835042	A2	19980813	WO 1998-US2485	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2279231	AA	19980813	CA 1998-2279231	19980206
AU 9863222	A1	19980826	AU 1998-63222	19980206
AU 737406	B2	20010816		
EP 966533	A1	19991229	EP 1998-907407	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001522228	T2	20011113	JP 1998-534982	19980206
US 6613740	B1	20030902	US 1998-187330	19981106
US 2004053313	A1	20040318	US 2003-623272	20030717
PRIORITY APPLN. INFO.:			US 1997-37404P	P 19970207
			WO 1998-US2485	W 19980206
			US 1998-187330	A3 19981106

AB The present invention relates generally to Activity Dependent Neurotrophic Factor III (ADNF III), also known as Activity Dependent Neuroprotective Protein (ADNP). More particularly, the present invention relates to nucleic acid sequences encoding ADNF III polypeptides; ADNF III polypeptides encoded by such nucleic acid sequences; antibodies to ADNF III polypeptides; and methods of using such ADNF III polypeptides for the treatment of neurol. deficiencies and for the prevention of cell death

Searcher : Shears 571-272-2528

associated with (1) gp120, the envelope protein from HIV; (2) N-methyl-D-aspartic acid (excito-toxicity); (3) tetrodotoxin (blockage of elec. activity); and (4) β -amyloid peptide, a substance related to neuronal degeneration in Alzheimer's disease. The rat and human ADNF III cDNAs were cloned and sequenced. ADNF III protected against tetrodotoxin and β -amyloid peptide toxicity at femtomolar concns. in cerebral cortical cultures. An ADNF III-derived octapeptide, NAPVSIPQ, mimicked the activity of the total protein in a neurodegeneration model system (ApoE-deficient homozygous mice) and a rat model of cholinergic deficiency.

IT 211439-10-0 211439-12-2

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ADNF III peptide; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT 211681-43-5 211681-48-0

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 15 Mar 1997

ACCESSION NUMBER: 1997:177635 CAPLUS

DOCUMENT NUMBER: 126:259561

TITLE: Antiserum to activity-dependent neurotrophic factor produces **neuronal cell death** in CNS cultures: immunological and biological specificity

AUTHOR(S): Gozes, Illana; Davidson, Ariane; Gozes, Yehoshua; Mascolo, Richard; Barth, Rolf; Warren, Dale; Hauser, Janet; Brenneman, Douglas E.

CORPORATE SOURCE: Department of Clinical Biochemistry, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel
SOURCE: Developmental Brain Research (1997), 99(2), 167-175
CODEN: DBRRDB; ISSN: 0165-3806

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) is a glia-derived protein that is neuroprotective at femtomolar concns. ADNF is released from astroglia after treatment with 0.1 nM vasoactive intestinal peptide (VIP). To further assess the biol. role of ADNF, antiserum was produced following sequential injections of purified ADNF into mice. Anti-ADNF ascites fluid (1:10,000) decreased neuronal survival by 45-55% in comparison to untreated cultures or those treated with control ascites. The neuronal death after anti-ADNF treatment was observed in cultures derived from the spinal cord, hippocampus or cerebral cortex at similar IC50's. Using a terminal deoxynucleotidyl transferase in situ assay to estimate apoptosis in cerebral cortical cultures, anti-ADNF was shown to produce a 70% increase

in the number of labeled cells in comparison to controls. In spinal cord cultures, anti-ADNF treatment produced a 20% decrease in choline acetyltransferase activity in comparison to controls. **Neuronal cell death** produced by the antiserum to ADNF was prevented in cultures co-treated with purified ADNF or ADNF-15, an active peptide derived from the parent ADNF. In vitro binding between the anti-ADNF and ADNF-15 was demonstrated with size exclusion chromatog. Comparative studies with other growth factors (insulin-like growth factor-1, platelet-derived growth factor, nerve growth factor, epidermal growth factor, ciliary neurotrophic growth factor, and neurotrophin-3) demonstrated that only ADNF prevented **neuronal cell death** associated with elec. blockade. These investigations indicated that an ADNF-like substance was present in cultures derived from multiple locations in the central nervous system and that ADNF-15 exhibited both neuroprotection and immunogenicity. ADNF appears to be both a regulator of activity-dependent neuronal survival and a neuroprotectant.

IT 188781-55-7

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(activity-dependent neurotrophic factor antiserum produces **neuronal cell death** in CNS cultures)

L3 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 22 Jun 1996

ACCESSION NUMBER: 1996:363612 CAPLUS

DOCUMENT NUMBER: 125:26945

TITLE: Neurotrophic peptides of activity dependent neurotrophic factor

INVENTOR(S): Brenneman, Douglas E.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611948	A1	19960425	WO 1995-US12929	19951016
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6174862	B1	20010116	US 1994-324297	19941017
CA 2202496	AA	19960425	CA 1995-2202496	19951016
AU 9537641	A1	19960506	AU 1995-37641	19951016
AU 707838	B2	19990722		
EP 797590	A1	19971001	EP 1995-935735	19951016
EP 797590	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10509428	T2	19980914	JP 1995-513344	19951016

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AT 212359 E 20020215 AT 1995-935735 19951016
PRIORITY APPLN. INFO.: US 1994-324297 A 19941017
US 1991-688087 B2 19910422
US 1992-871973 A2 19920422
WO 1995-US12929 W 19951016

AB The present invention relates generally to activity dependent neurotrophic factor (ADNF). More particularly, the present invention relates to a family of polypeptides derived from ADNF that exhibit neuroprotective/neuroprotective/neurotrophic action on neurons originating in the central nervous system and to uses thereof for the treatment of neurol. deficiencies and for the prevention of cell death. The present invention also relates to pharmaceutical compns. designed to prevent **neuronal cell death**.

IT 177159-38-5, VLGGGSALLRSIPA 177718-96-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuroprotective and neurotrophic peptides from activity dependent neurotrophic factor)

L3 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 30 May 1996

ACCESSION NUMBER: 1996:314250 CAPLUS

DOCUMENT NUMBER: 125:1603

TITLE: A femtomolar-acting neuroprotective peptide

AUTHOR(S): Brenneman, Douglas E.; Gozes, Illana

CORPORATE SOURCE: Natl. Institute Child Health and Human Development, Natl. Institutes Health, Bethesda, MD, 20892-4480, USA

SOURCE: Journal of Clinical Investigation (1996), 97(10), 2299-2307

CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel 14-amino acid peptide, with stress-protein-like sequences, exhibiting neuroprotection at unprecedented concns., is revealed. This peptide prevented **neuronal cell death** associated with the envelope protein (GP 120) from HIV, with excitotoxicity (NMDA), with the beta amyloid peptide (putative cytotoxin in Alzheimer's disease), and with tetrodotoxin (elec. blockade). The peptide was designed to contain a sequence derived from a new neuroprotective protein secreted by astroglial cells in the presence of vasoactive intestinal peptide. The neurotrophic protein was isolated by sequential chromatog. methods combining ion exchange, size separation, and hydrophobic interaction.

The protein (mol. mass, 14 kDa and pI, 8.3) was named activity-dependent neurotrophic factor, as it protected neurons from death associated with elec.

blockade. Peptide sequencing led to the synthesis of the novel 14-amino acid peptide that was homologous, but not identical, to an intracellular stress protein, heat shock protein 60. Neutralizing antiserum to heat shock protein 60 produced **neuronal cell death** that could be prevented by cotreatment with the novel protein, suggesting the existence of extracellular stress-like proteins with neuroprotective properties. These studies identify a potent neuroprotective glial protein and an active peptide that provide a basis for developing treatments of

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currently intractable neurodegenerative diseases.
IT 177159-38-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective peptide from activity-dependent neurotrophic factor
acts at femtomolar levels)

E1 THROUGH E33 ASSIGNED

FILE 'REGISTRY' ENTERED AT 10:38:12 ON 24 FEB 2005
L4 33 SEA FILE=REGISTRY ABB=ON PLU=ON (17718-96-6/BI OR 211439-12-
2/BI OR 177159-38-5/BI OR 211439-10-0/BI OR 209051-20-7/BI OR
209051-27-4/BI OR 292039-06-6/BI OR 292039-07-7/BI OR 292039-08
-8/BI OR 327157-61-9/BI OR 327157-62-0/BI OR 211681-43-5/BI OR
211681-48-0/BI OR 270084-37-2/BI OR 270084-38-3/BI OR 292039-03
-3/BI OR 292039-04-4/BI OR 292039-05-5/BI OR 188781-55-7/BI OR
223533-74-2/BI OR 270898-03-8/BI OR 270898-05-0/BI OR 320609-76
-5/BI OR 327157-63-1/BI OR 590465-44-4/BI OR 590465-45-5/BI OR
590465-46-6/BI OR 590465-47-7/BI OR 590465-48-8/BI OR 590465-49
-9/BI OR 590516-42-0/BI OR 590516-43-1/BI OR 590516-45-3/BI)

L5 33 L1 AND L4

L5 ANSWER 1 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 590516-45-3 REGISTRY
CN 26: PN: US6613740 SEQID: 41 unclaimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 800

SEQ 1 MVNRLSIPKP NLNSTGVNMM SSVHLQNNY GVKSVMGQYS VGQSMRLGLG
51 GNAFVSIPQQ SQSVKQLLPS GNGRSYGLGS EQRSQAPARY SLQSANASSL
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101	SSGHLKSPSL	SHSQASRVLG	QSSSKPAAAA	TGPPPGNTSS	TQKWKICTIC
151	NELFPENVYS	VHFEKEHKAE	KVPAVANYIM	KIHNTSKCL	YCNRYLPTDT
201	LLNHMLIHGL	SCPYCRSTFN	DVEKMAAHR	MVHIDEEMGP	KTDSTLSFDL
251	TLQQGSHTNI	HLLVTTYNLR	DAPAESVAYH	AQNNPPVPPK	PQPKVQEKAD
301	IPVKSSPQAA	VPYKKDVGKT	LCPLCFSILK	GPISDALAH	LRERHQVIQT
351	VHPVEKKLTY	KCIHCLGVYT	SNMTASTITL	HLVHCRGVGK	TQNGQDKTNA
401	PSRLNQSPSL	APVKRTYEQM	EFPLLKKRKL	DDSDSPSFF	EEKPEEPVVL
451	ALDPKGHEDD	SYEARKSFLT	KYFNKQPYPT	RREIEKLAAS	LWLWKS DIAS
501	HFSNKRKKCV	RDCEKYKPGV	LLGFNMKELN	KVKHEMDFDA	EWLFENHDEK
551	DSRVNASKTA	DKKLNLGKED	DSSDSFENL	EEESNESGSP	FDPVFVEVEPK
601	ISNDNP EEHV	LKVIPEDASE	SEEKLDQKED	GSKYETIHLT	EEPTKLMHNA
651	SDSEVDQDDV	VEWKDGASPS	ESGPGSQQVS	DFEDNTCEMK	PGTWSDESSQ
701	SEDARSSKPA	AKKKATMQGD	REQLKWKNSS	YGKVEGFWSK	DQSQWK NASE
751	NDERLSNPQI	EWQNSTIDSE	DGEQFDNMTD	GVTEPMHGSL	AGVKLSSQQA

HITS AT: 52-59

REFERENCE 1: 139:208245

L5 ANSWER 2 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 590516-43-1 REGISTRY
CN 24: PN: US6613740 SEQID: 32 unclaimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 781

SEQ 1 MSSVHLQNN YGVKSVMGQY SVGQSMRLGL GNAFVSIPQ SQSVKQLLPS

Searcher : Shears 571-272-2528

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 51 SGNRSYGLG SEQRSQAPAR YSLQSANASS LSSGHLKSPS LSHSQASRVL
101 GQSSSKPAAA ATGPPPGNTS STQKWKICTI CNELFPENVY SVHFEKEHKA
151 EKVPVANYI MKIHNFTSKC LYCNRYLPTD TLLNHMLIHG LSCPYCRSTF
201 NDVEKMAAHM RMVHIDEEMG PKTDSTLSFD LTLOQGSHTN IHLLVTTYNL
251 RDAPAESVAY HAQNNPPVPP KPQPKVQEKAD DIPVKSSPQA AVPYKKDVGK
301 TLCPLCFSIL KGPISDALAH HLRERHQVIQ TVHPVEKKLT YKCIHCLGVY
351 TSNMTASTIT LHLVHCRGVG KTQNGQDKTN APSRLNQSPS LAPVKRTYEQ
401 MEFPLLKKRK LDDSDSPSF FEEKPEEPVV LALDPKGHED DSYEARKSFL
451 TKYFNKQYPY TRREIEKLAA SLWLWKS DIA SHFSNKRKKC VRDCEKYKPG
501 VLLGFNMKEL NKVKHEMDFD AEWLFENHDE KDSRVNASKT ADKKLNLGKE
551 DDSSSDSFEN LEEESNESGS PFDPVFEVEP KISNDNPEEH VLKVIPEDAS
601 ESEKLDQKE DGSKYETIHL TEEPTKLMHN ASDSEVDQDD VVEWKDGASP
651 SESGPGSQV SDFEDNTCEM KPGTWSDESS QSEDARSSKP AAKKKATMQG
701 DREQLKWKNS SYGKVEGFWS KDQSQWKNAS ENDERLSNPQ IEWQNSTIDS
751 EDGEQFDNMT DGVTEPMHGS LAGVKLSSQQ A

HITS AT: 33-40

REFERENCE 1: 139:208245

L5 ANSWER 3 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 590516-42-0 REGISTRY
CN 23: PN: US6613740 SEQID: 31 unclaimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 787
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SEQ 1 MSNVHLQQNN YGVKSVGQSY GVGQSVRLGL GGNAPVSIPO QSQSVKQLLP
=====
 51 SGNRSFGLG AEQRPPAAAR YSLQTANTSL PPGQVKSPSV SQQASRVLG
101 QSSSKPPPA TGPSPNHCA TQKWKICTIC NELFPENVYS VHFEKEHKA
151 KVPVANYIM KIHNFSTKCL YCNRYLPTDT LLNHMLIHGL SCPYCRSTFN
201 DVEKMAAHMR MVHIDEEMGP KTDSTLSFDL TLQQGSHTNI HLLVTTYNLR
251 DAPAESVAYH AQNNAPVPPK PPKVQEKAD VPVKSSPQAA VPKKDVGKT
301 LCPLCFSILK GPISDALAHH LRERHQVIQT VHPVEKKLTY KCIHCLGVYT
351 SNMTASTITL HLVHCRGVGK TQNGQDKTNA PSRLNQSPGL APVKRTYEQM
401 EFPLLKKRKL EEDADSPSCF EEPPEEPVVL ALDPKGHEDD SYEARKSFLT
451 KYFNKQPYPT RREIEKLAAS LWLWKS DIAS HFSNKRKKCV RDCEKYKPGV
501 LLGFNMKELN KVKHEMDFDA EWLFEHDEK DSRVNASKTV DKKHNLGKED
551 DSFSDSFEHL EEESNGSGSP FDPVFEVEPK IPSDNLEEPV PKVIPEGALE
601 SEKLDQKEEE EEEEEEDGSK YETIHLTEEP AKLMHDASDS EVDQDDVVEW
651 KDGASPSSEG PGSQQISDFE DNTCEMKPGT WDESSQSED ARSSKPAACK
701 KATVQDDTEQ LKWKNSSYGK VEGFWSKDQS QWENASENAE RLPNPQIEWQ
751 NSTIDSEGE QFDSMTDGVA DPMHGS LTGV KLSSQQA

HITS AT: 33-40
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REFERENCE 1: 139:208245

L5 ANSWER 4 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 590465-49-9 REGISTRY
CN Activity-dependent neurotrophic factor III (Mus musculus 828-amino acid
isoform) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 29: PN: US6613740 SEQID: 55 claimed protein
CI MAN
SQL 828
```

Searcher : Shears 571-272-2528

09/267511

SEQ 1 MGLPPRISSL ASGNVRS LPS QQMVNRLSIP KPNLNSTGVN MMSNVHLQQN
51 NYGVKSVGQS YGVGQSVRLG LGGNAPVSIP QQSQSVKQLL PSGNGRSFGL
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101 GAEQRPPAAA RYSLQTANTS LPPGQVKSPS VSQSQASRVL GQSSSKPPPA
151 ATGPPPSNHC ATQKWKICTI CNELFPENVY SVHFEKEHKA EKVPVANYI
201 MKIHNFTSKC LYCNRYLPTD TLLNHMLIHG LSCPYCRSTF NDVEKMAAHM
251 RMVHIDEEMG PKTDSTLSFD LTLQQGSHTN IHLLVTTYNL RDAPAESVAY
301 HAQNNAPVPP KPQPKVQEK DVPVKSSPQA AVPYKKDVGK TLCPLCFSIL
351 KGPISDALAH HLRERHQVIQ TVHPVEKKLT YKCIHCLGVY TSNMTASTIT
401 LHLVHCRGVG KTQNGQDKTN APSRLNQSPG LAPVKRTYEQ MEFPLLKKRK
451 LEEDADSPSC FEEKPEEPVV LALDPKGHE DSYEARKSFL TKYFNKPYP
501 TRREIEKLAA SLWLWKS DIA SHFSNKRKKC VRDCEKYKPG VLLGFNMKEL
551 NKVKHEMDFD AEWLFENHDE KDSRVNASKT VDKKHNLGKE DDSFSDSFEH
601 LEEESNGSGS PFDPVFEVEP KIPSDNLEEP VPKVIPEGAL ESEKLDQKEE
651 EEEEEEDGS KYETIHLTEE PAKLMHDASD SEVDQDDVVE WKDGASPSSES
701 GPGSQQISDF EDNTCEMKPG TWSDESSQSE DARSSKPAK KKATVQDDTE
751 QLKWKNSSYG KVEGFWSKDQ SQWENASENA ERLPNPQIEW QNSTIDS EDG
801 EHFDSMTDGV ADPMHGS L TG VKLSSQQA

HITS AT: 74-81

REFERENCE 1: 139:208245

L5 ANSWER 5 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 590465-48-8 REGISTRY

CN Activity-dependent neurotrophic factor III (Mus musculus 806-amino acid isoform) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 10: PN: US6613740 SEQID: 3 claimed protein

CI MAN

SQL 806

SEQ 1 MVNRLSIPKP NLNSTGVNMM SNVHLQQNNY GVKSVGQSYG VGQSVRLGLG
51 GNA PVSIPQQ SQSVKQLLPS GNGRSFGLGA EQRPPAAARY SLQTANTSLP
===== =
101 PGQVKSPSVS QSQASRVLGQ SSSKPPPAAT GPPPSNHCAT QKWKICTICN
151 ELFPENVYSV HFEKEHKA EK VPAVANYIMK IHNFTSKCLY CNRYLPTDTL
201 LNHMLIHGLS CPYCRSTFND VEKMAAHMRM VHIDEEMGPK TDSTLSFDLT
251 LQQGSHTNIH LLVTTYNL RD APAESVAYHA QNNAPVPPKP QPKVQEKADV
301 PVKSSPQAAV PYKKDVGKTL CPLCFSILKG PISDALAHHL RERHQVIQTV
351 HPVEKKLT YK CIHCLGVYTS NMTASTITLH LVHCRGVGKT QNGQDKTNAP
401 SRLNQSPGLA PVKRTYEQME FPLLKKRKLE EDADSPSCFE EKPEEPVVL A
451 LDPKGHEDDS YEARKSFLTK YFNKPYPTR REIEKLAASL WLWKS DIASH
501 FSNKRKKCV R DCEKYKPGVL LGFNMKELNK VKHEMDFDAE WLFENHDEKD
551 SRVNASKTV D KKHNLGKEDD SFSDSFEHLE EESNGSGSPF DPVFEVEPKI
601 PSDNLEEPVP KVIPEGAL ESEKLDQKEEEE EEEEEEDGSKY ETIHLTEEPA
651 KLMHDASDSE VDQDDVVEWK DGASPSSESGP GSQQISDFED NTCEMKPGTW
701 SDESSQSEDA RSSKPAAKKK ATVQDDTEQL KWKNSSYGKV EGFWSKDQSQ
751 WENASENAER LPNPQIEWQN STIDS EDGEQ FDSMTDGVAD PMHGS L TG VK
801 LSSQQA

HITS AT: 52-59

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:208245

L5 ANSWER 6 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

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RN 590465-47-7 REGISTRY
CN Activity-dependent neurotrophic factor III (human clone H7) (9CI) (CA
INDEX NAME)

OTHER NAMES:

CN 33: PN: US6613740 SEQID: 59 claimed protein
CI MAN
SQL 874

SEQ 1 MPKSYEALVQ HVIEDHERIG YQVTAMIGHT NVVVPRSKPL MLIAPKPQDK
51 KSMGLPPRIG SLASGNVRSI PSQQMVNRLS IPKPNLNSTG VNMSSSVHLQ
101 QNNYGVKSVG QGYSVGQSMR LGLGGNAPVS IPQQSQSVKQ LLPSGNGRSY
===== ===
151 GLGSEQRSQA PARYSLQSAN ASSLSGQLK SPSLSQSQAS RVLGQSSSKP
201 AAAATGPPPG NTSSTQKWKI CTICNELFPE NVYSVHFEKE HKAEKVPAVA
251 NYIMKIHNFT SKCLYCNRYL PTDTLLNHML IHGLSCPYCR STFNDVEKMA
301 AHMRMVHIDE EMGPKTDSTL SFDLTLLQGS HTNIHLLVTT YNLRDAPAES
351 VAYHAQNNPP VPPKPQPKVQ EKADIPVKSS PQAAVPYKQD VGKTLCPCLCF
401 SILKGPISTA LAHHLRERHQ VIQTVHPVEK KLTYKCIHCL GVYTSNMTAS
451 TITLHLVHCR GVGKTQNGQD KTNAPSRLNQ SPSLAPVKRT YEQMEFPLLK
501 KRKLDDSDS PSFFEEKPEE PVVLALDPKG HEDDSYEARK SFLTIFYFNKQ
551 PYPTRREIEK LAASLWLWKS DIASHFSNKR KKCVRDCEKY KPGVLLGFNM
601 KELNKVKHEM DFDAEWLFEN HDEKDSRVNA SKTADKKLNL GKEDDSSSDS
651 FENLEESNE SGSPFDPVFE VEPKISNDNP EEHVLKVIPE DASESEEKLD
701 QKEDGSKYET IHLTEEPTKL MHNASDSEVD QDDVVEWKDG ASPSESGPGS
751 QQVSDFFEDNT CEMKPGTWS D ESSQSEDARS SKPAAKKKAT MQGDREQLKW
801 KNSSYGKVEG FWSKDQSQWK NASENDERLS NPQIEWQNST IDSEDGEQFD
851 NMTDGVAEPM HGSLAGVKLS SQQA

HITS AT: 126-133

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:208245

L5 ANSWER 7 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 590465-46-6 REGISTRY
CN Activity-dependent neurotrophic factor III (human clone H3) (9CI) (CA
INDEX NAME)

OTHER NAMES:

CN 31: PN: US6613740 SEQID: 57 claimed protein
CI MAN
SQL 726

SEQ 1 RSLPSQQMVN RLSIPKPNLN STGVNMMSSV HLQQNNYGVK SVGQGYSVGQ
51 SMRLGLGGNA PVSIPQQSQS VKQLLPSGNG RSYGLGSEQR SQAPARYSLQ
== =====
101 SANASSLSSG QLKSPSLSQS QASRVLGQSS SKPAAAATGP PPGNTSSTQK
151 WKICTICNEL FPENVYSVHF EKEHKAQKVP AVANYIMKIH NFTSKCLYCN
201 RYLPTDTLLN HMLIHGLSCP YCRSTFNDVE KMAAHMRMVH IDEEMGPKTD
251 STLSTLTLQ QGSHTNIHLL VTTYNLRDAP AESVAYHAQN NPPVPPKPQ
301 KVQEKADIPV KSSPQAAVPY KKDVGKTLCP LCFSILKGPI SDALAHHLRE
351 RHQVIQTVHP VEKKLTYKCI HCLGVYTSNM TASTITLHLV HCRGVGKTQN
401 GQDKTNAPSR LNQSPSLAPV KRTYEQMEFP LLKKRKLDDD SDSPSFFEEK
451 PEEPVLALD PKGHEDDSYE ARKSFLTIFY NKQPYPTRRE IEKLAASLWL
501 WKSDIASHFS NKRKKCVRDC EKYKPGVLLG FNMKELNKVK HEMDFDAEWL
551 FENHDEKDSR VNASKTADKK LNLGKEDDSS SDSFENLEEE SNESGSPFDP
601 VFEVEPKISN DNPEEHVLKV IPEDASESEE KLDQKEDGSK YETIHLTEEP

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651 TKLMHNASDS EVDQDDVVEW KDGASPSSEG PGSQQVSDFE DNTCEMKPGT
701 WSESSQSED ARSSKPAACK KGYHAR
HITS AT: 59-66

REFERENCE 1: 139:208245

L5 ANSWER 8 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 590465-45-5 REGISTRY
CN Activity-dependent neurotrophic factor III (human clone H3') (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN 8: PN: US6613740 SEQID: 1 claimed protein
CI MAN
SQL 1000

SEQ 1 MVNRLSIPKP NLNSTGVNMM SSVHLQNNY GVKSVGQGYG VGQSMRLGLG
51 GNAPVSIPQQ SQSVKQLLPS GNGRSYGLGS EQRSQAPARY SLQSANASSL
=====

101 SSGHLKSPSL SHSQASRVLG QSSSKPAAAA TGPPPGNTSS TQKWIKICTIC
151 NELFPENVYS VHFKEHKAE KVPVANYIM KIHNFSTKCL YCNRYLPTDT
201 LLNHMLIHGL SCPYCRSTFN DVEKMAAHR MVHIDEEMGP KTDSTLSFDL
251 TLQGSHTNI HLLVTTYNLR DAPAESVAYH AQNNPPVPPK PQPKVQEKAD
301 IPVKSSPQAA VPKKDVGKT LCPLCFSILK GPISDALAHH LRERHQVIQT
351 VHPVEKKLTY KCIHCLGVYT SNMTASTITL HLVHCRGVGK TQNGQDKTNA
401 PSRLNQSPSL APVKRTYEQM EFPLLKKRKL DDDSDSPSFF EEKPEEPVVL
451 ALDPKGHEDD SYEARKSFLT KYFNKQPYPT RREIEKLAAS LWLWKS DIAS
501 HFSNKRKKCV RDCEKYKPGV LLGFNMKELN KVKHEMDFDA EWLFEHDEK
551 DSRVNASKTA DKKLNLGKED DSSSDSFENL EEESNESGSP FDPVFEVEPK
601 ISNDNPEEHV LKVIPEDASE SEEKLDQKED GSKYETIHLT EEPTKLMHNA
651 SDSEVDQDDV VEWKDGASPS ESGPGSQQVS DFEDNTCEMK PGTWSESSQ
701 SEDARSSKPA AKKKATMQGD REQLKWKNS YGKVEGFWSK DQSQWKNAE
751 NDERLSNPQI EWQNSTIDSE DGEQFDNMTD GVTEPMHGSL AGVKLSSQQA
801 XVPGLALVT CCSLELXSPV XLQSCLLTGT ALXVLVGLWG MWPLQFQWLF
851 LSLXQDRLFL LQNLXQTRX LNVKNQXAGD SXILTRKSRG LFLSAFSTFL
901 SLCEMIGQMS LRSVKLIHMV VXGQHTSYQS NVYSRLWEKR FFFMYSFXIV
951 EMYICTVFXT YSKXCSXSCY CVPIIDFFFX CCPCCVINAL SSLPSKSSKL

HITS AT: 52-59

REFERENCE 1: 139:208245

L5 ANSWER 9 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 590465-44-4 REGISTRY
CN 15: PN: US6613740 SEQID: 10 claimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 88

SEQ 1 XXXXXXXXXXX XXXXXXXXXXX XXXXXXXXXXX XXXXXXXXXXX NAPVSIPQXX
=====

51 XXXXXXXXXXX XXXXXXXXXXX XXXXXXXXXXX XXXXXXXXXXX

HITS AT: 41-48

REFERENCE 1: 139:208245

L5 ANSWER 10 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 327157-63-1 REGISTRY
CN D-Glutamine, D-asparaginy-D-alanyl-L-prolyl-D-valyl-D-seryl-D-isoleucyl-D-

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SQL prolyl- (9CI) (CA INDEX NAME)
8

SEQ 1 NAPVSIPO
=====

HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 134:198025

L5 ANSWER 11 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 327157-62-0 REGISTRY
CN D-Glutamine, D-asparaginyl-D-alanyl-D-prolyl-D-valyl-D-seryl-D-isoleucyl-D-
prolyl- (9CI) (CA INDEX NAME)
CI COM
SQL 8

SEQ 1 NAPVSIPO
=====

HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 141:201591

REFERENCE 2: 141:64409

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

L5 ANSWER 12 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 327157-61-9 REGISTRY
CN D-Alanine, D-seryl-D-alanyl-D-leucyl-D-leucyl-D-arginyl-D-seryl-D-
isoleucyl-D-prolyl- (9CI) (CA INDEX NAME)
CI COM
SQL 9

SEQ 1 SALLRSIPA
=====

HITS AT: 1-9

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 141:201591

REFERENCE 2: 141:64409

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

L5 ANSWER 13 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 320609-76-5 REGISTRY
CN Peptide, (Xaa-Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala-Xaa) (9CI) (CA INDEX

Searcher : Shears 571-272-2528

09/267511

NAME)
OTHER NAMES:
CN 1: PN: US6174862 SEQID: 16 claimed protein
CI MAN
SQL 11

SEQ 1 XSALLRSIPA X
=====

HITS AT: 2-10

REFERENCE 1: 134:120910

L5 ANSWER 14 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 292039-08-8 REGISTRY
CN L-Serine, L-leucylglycyl-L-leucylglycylglycyl-L-asparaginyL-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl-L-glutaminyL-L-glutaminyL-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN 18: PN: US6613740 SEQID: 35 unclaimed protein
CN 23: PN: WO2004080957 SEQID: 11 claimed sequence
CN 7: PN: WO2004060309 SEQID: 4 claimed protein
SQL 15

SEQ 1 LGLGGNAPVS IPQQS
=====

HITS AT: 6-13

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

L5 ANSWER 15 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN 292039-07-7 REGISTRY
CN L-Serine, L-leucylglycylglycyl-L-asparaginyL-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl-L-glutaminyL-L-glutaminyL-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN 17: PN: US6613740 SEQID: 34 unclaimed protein
CN 22: PN: WO2004080957 SEQID: 10 claimed sequence
CN 6: PN: WO2004060309 SEQID: 3 claimed protein
SQL 13

SEQ 1 LGGNAPVSIP QQS
=====

HITS AT: 4-11

REFERENCE 1: 141:289067

09/267511

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

L5 ANSWER 16 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 292039-06-6 REGISTRY

CN L-Glutamine, glycylglycyl-L-asparaginyl-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 10: PN: WO2004060309 SEQID: 20 claimed protein

CN 16: PN: US6613740 SEQID: 33 unclaimed protein

CN 21: PN: WO2004080957 SEQID: 9 claimed sequence

SQL 10

SEQ 1 GGNAPVSIPO

=====

HITS AT: 3-10

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

L5 ANSWER 17 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 292039-05-5 REGISTRY

CN L-Alanine, glycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 19: PN: WO2004080957 SEQID: 7 claimed sequence

CN 4: PN: WO2004060309 SEQID: 18 claimed protein

SQL 11

SEQ 1 GGSALLRSIP A

=====

HITS AT: 3-11

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

Searcher : Shears 571-272-2528

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REFERENCE 5: 133:233267

L5 ANSWER 18 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 292039-04-4 REGISTRY

CN L-Alanine, glycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 18: PN: WO2004080957 SEQID: 6 claimed sequence

CN 3: PN: WO2004060309 SEQID: 17 claimed protein

SQL 12

SEQ 1 GGGSALLRSI PA

===== ==

HITS AT: 4-12

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

REFERENCE 5: 133:233267

L5 ANSWER 19 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 292039-03-3 REGISTRY

CN L-Alanine, L-leucylglycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 17: PN: WO2004080957 SEQID: 5 claimed sequence

CN 2: PN: WO2004060309 SEQID: 16 claimed protein

SQL 13

SEQ 1 LGGSALLRS IPA

===== ==

HITS AT: 5-13

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

REFERENCE 5: 133:233267

L5 ANSWER 20 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN

RN 270898-05-0 REGISTRY

CN 32: PN: WO0027875 FIGURE: 13 unclaimed sequence (9CI) (CA INDEX NAME)

CI MAN

SQL 874

SEQ 1 MPKSYEALVQ HVIEDHERIG YQVTAMIGHT NVVVPRSKPL MLIAPKPQDK

Searcher : Shears 571-272-2528